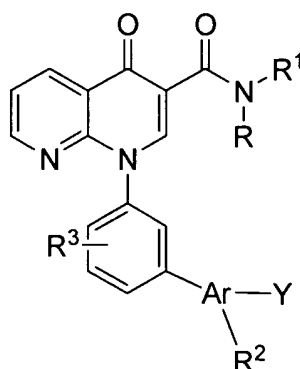


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listing of claims in the application.

1. (Canceled)
2. (Previously amended) A compound represented by Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

Ar is phenyl, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, or imidazolyl; or oxides thereof when Ar is a heteroaryl;

Y is -COOH, or -C₁₋₆alkyl(C₁₋₄alkyl)_n-COOH, wherein the -C₁₋₆alkyl is optionally substituted with halogen, alkoxy, hydroxy or nitrile, and the (C₁₋₄alkyl) substituents are optionally linked to form a C₃₋₄cycloalkyl; wherein n is 0, 1, 2, 3 or 4;

R is H or -C₁₋₆alkyl;

R¹ is H, or -C₁₋₆alkyl, -C₃₋₆cycloalkyl, -C₁₋₆alkoxy, -C₂₋₆alkenyl, -C₃₋₆alkynyl, heteroaryl, or heterocycle group, optionally substituted with 1-3 independent haloC₁₋₆alkyl, -C₁₋₆alkyl, -C₁₋₆alkoxy, OH, amino, -(C₀₋₆alkyl)-SO_p-(C₁₋₆alkyl), nitro, CN, =N-O-C₁₋₆alkyl, -O-N=C₁₋₆alkyl, or halogen substituents, wherein p is 0, 1 or 2;

R² is H, halogen, -CN, -NO₂, -C₁₋₆alkyl, -C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, O-C₁₋₆alkyl, O-C₃₋₆cycloalkyl-C₁₋₆alkyl(C₃₋₆cycloalkyl)(C₃₋₆cycloalkyl), -C₁₋₆alkoxy, phenyl, heteroaryl, heterocycle, amino, -C(O)-C₁₋₆alkyl, -C(O)-O-C₁₋₆alkyl, -C₁₋₆alkyl(=N-OH), -C(N=NOH)C₁₋₆alkyl, -C₀₋₆alkyl(oxy)C₁₋₆alkyl-phenyl, -SO_kNH(C₀₋₆alkyl), or -(C₀₋₆alkyl)-SO_k-(C₁₋₆alkyl), wherein the phenyl, heteroaryl or heterocycle is optionally substituted with halogen, -C₁₋₆alkyl, -C₁₋₆alkoxy, hydroxy, amino,

or -C(O)-O-C₁₋₆alkyl, and wherein the alkyl or cycloalkyl is optionally substituted with 1-6 independently selected halogens or -OH, and wherein k is 0, 1, or 2;

R³ is selected from H, halogen, CN, -C₁₋₆alkyl, -C₃₋₆cycloalkyl, nitro, -C(O)-C₁₋₆alkyl, -C(O)-O-C₀₋₆alkyl, -SO_{n'}NH(C₀₋₆alkyl), or -(C₀₋₆alkyl)-SO_{n'}-(C₁₋₆alkyl), O-C₁₋₆alkyl, O-C₃₋₆cycloalkyl, wherein n' is 0, 1, or 2 and wherein the alkyl and cycloalkyl is optionally substituted with 1-6 independently selected halogen or OH.

3 to 10. (Canceled)

11. (Original) The compound according to claim 2, or a pharmaceutically acceptable salt, wherein

Ar is pyridyl, pyrimidyl, or oxide thereof.

12. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt, wherein

R¹ is -C₁₋₆alkyl optionally substituted with 1-3 independent -C₁₋₆alkyl, -C₁₋₆alkoxy, OH, amino, -(C₀₋₆alkyl)-SO_p-(C₁₋₆alkyl), nitro, CN, =N-O-C₁₋₆alkyl, -O-N=C₁₋₆alkyl, or halogen substituents.

13. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R¹ is -C₃₋₆cycloalkyl optionally substituted with 1-3 independent -C₁₋₆alkyl, -C₁₋₆alkoxy, OH, amino, -(C₀₋₆alkyl)-SO_p-(C₁₋₆alkyl), nitro, CN, =N-O-C₁₋₆alkyl, -O-N=C₁₋₆alkyl, or halogen substituents.

14. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R is hydrogen.

15. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R² is hydrogen or -C₁₋₃alkyl or halogen.

16. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R¹ is -C₃₋₆cycloalkyl optionally substituted with methyl or halo; and

R is hydrogen.

17. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R¹ is cyclopropyl optionally substituted with methyl or halo; and

R and R² are hydrogen or halogen;

R³ is hydrogen or halogen.

18. (Original) The compound according to claim 2, or a pharmaceutically acceptable salt thereof, wherein

R and R³ are hydrogen,;

R¹ is -C₃₋₆cycloalkyl optionally substituted with methyl or halo, or -C₁₋₃alkyl optionally substituted with 1-3 halo; and

Ar is phenyl.

19. (Canceled)

20. (Currently Amended) The compound which is
2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;
2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;
2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}-2-methylpropanoic acid;
2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2-methylpropanoic acid;
3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-3-methylbutanoic acid;
{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}(hydroxy)acetic acid;
1-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;
2-(cis)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

5-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid;

1-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

1-cyano-3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2,2-dimethylcyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-fluoro-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

(cis)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-bromo-5'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-methyl-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-2-methyl-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(cis)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-fluoro-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-carboxylic acid;

2-(trans)-{3'-[3-(morpholin-4-ylcarbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[4-oxo-3-({[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino}carbonyl)-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-({[2-(methylthio)ethyl]amino}carbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-({[2-(methylsulfonyl)ethyl]amino}carbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[4-oxo-3-({[2,2,2-trifluoroethyl]amino}carbonyl)-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-(5-{3-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]phenyl}thien-2-yl)cyclopropanecarboxylic acid;
2-(trans)-{3'-[3-{[(cyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;
2-(trans)-{3'-[3-{[(1-cyanocyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid; or
3-{3'-[3-[(isopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-3-methylbutanoic acid, or a pharmaceutically acceptable salt thereof.

21. (Currently amended) A The compound which is

(+)-(trans)-2-{3-fluoro-3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}methyl)cyclobutanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2-methylcyclopropanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}cyclopropanecarboxylic acid;
3-methyl-3-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}butanoic acid;
(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}cyclopropanecarboxylic acid;
(trans)-2-{3'-[4-oxo-3-{[(2,2,3,3,3-pentafluoropropyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-1-fluorocyclopropanecarboxylic acid;
(+)-(trans)-2-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
(-)-(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-ethyl 2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}cyclopropanecarboxylate;
(+)-(trans)-isopropyl 2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}cyclopropanecarboxylate;
tert-butyl 3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}-2,2-dimethylpropanoate;
3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}-2,2-dimethylpropanoic acid;
3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-3-yl}-2,2-dimethylpropanoic acid;
1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-3-yl}methyl)cyclobutanecarboxylic acid;
3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-2-yl}-2,2-dimethylpropanoic acid;
1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-2-yl}methyl)cyclobutanecarboxylic acid;
(+)-(trans)-2-{3'-[3-[(*tert*-butylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
(+)-(trans)-2-{3'-[3-[(cyclobutylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}bicyclo[1.1.1]pentane-1-carboxylic acid;
4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}-4-hydroxypentanoic acid;
~~(trans)-2-{3'-[3-[(\square)-cis-(2-fluorocyclopropyl)amino]carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;~~
(trans)-2-{3'-[3-[(\pm)-cis-(2-fluorocyclopropyl)amino]carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;
(+)-(trans)-2-{3'-[3-[(dicyclopropylmethyl)amino]carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4H)-yl]biphenyl-4-yl}-2,2-dimethylbutanoic acid;

(+)-(trans)-2-{3'-[3-{[(1-hydroxycyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[4-oxo-3-{[(1-phenylcyclopropyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

4-{3'-[3-{[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-3,3-dimethylbutanoic acid;

(+)-(trans)-2-{3'-[3-{[(1-cyclopropyl-1-methylethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

1-({3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}methyl)cyclobutanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(cyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(-)-(trans)-2-{3-fluoro-3'-[3-{[(1-hydroxycyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

~~(trans)-2-{3'-[4-oxo-3-{[(\square)-2,2,2-trifluoro-1-methylethyl]amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;~~

(trans)-2-{3'-[4-oxo-3-{[(\pm)-2,2,2-trifluoro-1-methylethyl]amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(1-methylcyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

2,2-dimethyl-4-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}butanoic acid;

2,2-dimethyl-3-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}propanoic acid;

(-)-(trans)-2-{3-chloro-3'-[3-{[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid; or

(+)-(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid, or a pharmaceutically acceptable salt thereof.

22. (Previously amended) A pharmaceutical composition comprising
a therapeutically effective amount of the compound according to claim 2 or a pharmaceutically acceptable salt thereof; and
a pharmaceutically acceptable carrier.

23 to 24. (Canceled).

25. (Previously amended) A method of treatment or prevention of asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), eosinophilic granuloma, psoriasis and other benign or malignant proliferative skin diseases, endotoxic shock (and associated conditions such as laminitis and colic in horses), septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, inflammatory arthritis, osteoporosis, chronic glomerulonephritis, atopic dermatitis, urticaria, adult respiratory distress syndrome, infant respiratory distress syndrome, chronic obstructive pulmonary disease in animals, diabetes insipidus, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, arterial restenosis, atherosclerosis, neurogenic inflammation, pain, cough, rheumatoid arthritis, ankylosing spondylitis, transplant rejection and graft versus host disease, hypersecretion of gastric acid, bacterial, fungal or viral induced sepsis or septic shock, inflammation and cytokine-mediated chronic tissue degeneration, osteoarthritis, cancer, cachexia, muscle wasting, depression, memory impairment, monopolar depression, acute and chronic neurodegenerative disorders with inflammatory components, Parkinson disease, Alzheimer's disease, spinal cord trauma, head injury, multiple sclerosis, tumour growth and cancerous invasion of normal tissues comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 2 or a pharmaceutically acceptable salt thereof.

26. (Previously amended) A method of enhancing cognition in a healthy subject comprising administering a safe cognition enhancing amount of compound according to claim 2, or a pharmaceutically salt thereof.

27 to 34. (Canceled)